REFRACTORY SYMPTOMS AND PALLIATIVE SEDATION
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REFRACTORY SYMPTOMS AND PALLIATIVE SEDATION THERAPY (PST)

This guideline is intended for use alongside consultation with experienced palliative care physicians/specialists and inter-professional palliative care teams.\(^1\),\(^2\),\(^3\) If there are no local palliative care physicians available, one can be reached via the BC Provincial Palliative Care Consultation Line (toll-free, 24/7): 1-877-711-5757 (accessible only for physicians and nurse practitioners).

Organizational policies about who may prescribe, administer and monitor Palliative Sedation Therapy (PST) vary throughout British Columbia. Before applying this guideline, ensure the appropriate personnel are involved as required for your organization.

DEFINITIONS:

**Palliative Sedation Therapy (PST):** The monitored use of pharmacological agent(s) to intentionally reduce consciousness to treat refractory, intractable and intolerable symptoms for a patient\(^1\) at end of life with advanced life-limiting, progressive illness.\(^5\),\(^4\) It is considered a last resort and is only used when other treatments have failed.\(^5\),\(^6\),\(^7\),\(^8\) The level of sedation must be in proportion to symptom severity, using the lowest dose to achieve comfort.\(^5\),\(^8\)

PST almost always continues until natural death from the illness occurs. This guideline does not encompass respite, temporary intentional, procedural, or intermittent sedation.\(^5\),\(^6\),\(^9\),\(^10\) If these are being considered, seek guidance from an experienced palliative care physician/specialist.

Sedation as a side effect of treatment (i.e., consequential sedation) is not PST. Decreased level of consciousness is expected in the natural dying process regardless of PST.\(^3\),\(^5\)

**The intent of PST is to provide symptom relief.** When used appropriately, it does not hasten death.\(^3\),\(^5\),\(^7\),\(^10\),\(^11\) While some patients with refractory symptoms may consider Medical Assistance in Dying (MAiD), the two are distinguished by their **intent** and **patient eligibility**, and these distinctions should be made clear to the patient, family and health care team.\(^1\),\(^2\),\(^5\),\(^6\),\(^12\) For guidance when responding to an expressed wish for hastened death, see Nurturing psychosocial and spiritual well-being - "Expressed wish to hasten death" on page 14

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\(^1\) "Patient” indicates the person receiving care and includes terms such as “client” and “resident”.

"Family” is defined by the person receiving care and includes all who are identified by them as significant and involved.
**Refractory Symptoms & Palliative Sedation**

<table>
<thead>
<tr>
<th>Palliative Sedation Therapy (PST)</th>
<th>Medical Assistance in Dying (MAiD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suffering is unbearable for the patient.</td>
<td>Suffering is unbearable for the patient.</td>
</tr>
<tr>
<td>Intent is to provide symptom management and relief of suffering.</td>
<td>Intent is to end life to relieve suffering.</td>
</tr>
<tr>
<td>Natural death from illness is imminent.⁴, ⁵, ⁶, ⁷</td>
<td>Natural death from illness is “reasonably foreseeable”.¹³</td>
</tr>
<tr>
<td>All other palliative interventions have been considered and are not possible or acceptable.</td>
<td>The patient has been made aware of means that are available to potentially relieve their suffering, including palliative care.¹³</td>
</tr>
<tr>
<td>Consent is required.</td>
<td>Consent is required.</td>
</tr>
<tr>
<td>Does not require that the patient be competent to provide consent. The Substitute Decision Maker (SDM) may consent on the patient’s behalf.</td>
<td>Requires that the patient is competent to provide consent at the time of administration.</td>
</tr>
</tbody>
</table>

**Table 1: Distinguishing between PST and MAiD**

**Refractory symptom(s):** the degree of suffering is unbearable for the patient and, after a thorough assessment, further interventions are determined to include one or any combination of the following:³, ⁴, ⁵

- Inaccessible or incapable of relieving suffering,
- Associated with unacceptable side effects,
- Unlikely to be effective within a reasonable time frame,⁵
- Not in keeping with the patient’s goals of care,⁵ and/or
- Unacceptable to the patient and/or family for other reasons.

Before determining if a symptom is refractory rather than difficult, a full assessment and advanced symptom management must be done in consultation with an experienced palliative care physician/specialist.³, ⁴ See [Assessment section](#) in following pages for details.
PREVALENCE

It is difficult to determine the prevalence of true refractory symptoms or the frequency of PST provision, both of which vary widely between care settings and jurisdictions. The reported percentages may be influenced by the availability of palliative experts and other resources, as well as local practice patterns and definitions.3, 7

IMPACT

Unrelieved symptoms cause suffering and distress to patients, their family members, and health care professionals.9, 14 It is crucial to include family in decision-making in order to mitigate the potential negative impact of a decision they don’t completely understand or agree with.7, 9, 15, 16 However, PST is only offered in response to a patient’s suffering, not to others’ discomfort or perceptions.3, 8

STANDARD OF CARE:

Step 1 | Goals of care conversations

When considering PST, goals of care conversations must have already taken place with readily accessible documentation. The patient’s goals of care must be to allow natural dying with a focus on comfort and symptom management. The patient and/or SDM must have an understanding and acceptance of the patient’s limited life-expectancy4, 5, 6, 7, 17 as further life-prolonging treatments, such as antibiotics and disease modifying agents, are typically stopped with the initiation of PST (unless they also contribute to symptom relief).

Decisions about the following interventions should be made in light of the limited prognosis and considered separately from the decision to proceed with PST: artificial hydration or nutrition, vital sign measurement, bowel and bladder interventions.4 Hydration is not usually offered but may be in some circumstances. 3, 5, 6, 7 Bowel interventions can likely be stopped, and urinary catheterization is only indicated with palpable bladder distention and signs of patient discomfort. 5, 7
Step 2 | Assessment

Determining that the criteria for PST are met requires knowledge of the patient and diagnosis, as well as symptom management expertise. For these reasons, it is strongly recommended that consultation with an experienced palliative care physician/specialist and inter-professional team be sought before deciding that a symptom is refractory in order to determine if PST is appropriate.

1. A thorough assessment of physical, mental, spiritual, and emotional health is needed to determine the nature of suffering.

2. Ensure all available supportive and symptom management interventions have been explored in consultation with experienced palliative care physicians/specialists and inter-professional team members.

3. Ask about and attend to the patient’s individual, family, community, and cultural values and beliefs. Some areas to ask about are: the meaning of suffering to them, beliefs about dying, importance of consciousness to the dying process (what are they willing to trade off for comfort), and cultural death rituals, ceremonies or spiritual practices.

Indications:

Indications for PST are intractable physical symptoms. For example: dyspnea, pain, nausea, delirium, and seizures.

Use of PST as a management for refractory psychological or spiritual distress without accompanying physical symptoms is controversial and requires consultation with inter-professional team members including social workers, spiritual health practitioners, traditional healers, and/or counsellors as appropriate and desired by the patient. Comply with your organization’s policies if considering PST in this situation.

Criteria required for PST are (See Appendix A for printable checklist):

- The patient has an advanced life-limiting, progressive illness with a limited prognosis, and death is estimated to be imminent within days.
- The symptom(s) are refractory and intolerable to the patient.
- A Do Not Resuscitate (DNR) order is in place. This may be contained within a Medical Order for Scope of Treatment (MOST) or another document.
- The patient or SDM has provided documented, informed consent.
In addition to assessing the patient, assess if the care setting is appropriately resourced. See Appendix A for a printable checklist for assessment of the care setting. If the current care setting is not able to support PST, transfer to another setting is required; this may be a factor to consider during decision-making as described below.

Step 3 | Decision-making

Once it is determined that the criteria have been met, then a decision is made about whether to proceed with PST. The decision must be made in consultation with the patient (when capable), family and/or their SDM, and inter-professional team members. Whenever possible, these discussions should happen in anticipation of refractory symptoms, before a crisis begins or escalates.

Patient, family and team meeting(s):

1. Empathically address the impact of unrelieved suffering on the patient and family.
2. Confirm the patient and/or family’s understanding of the limited prognosis.
3. Discuss all options, including risks and benefits. Ensure the patient and family have their questions answered.
4. Confirm current goals of care. If the patient is unable to communicate, ask their SDM if they have shared their values, beliefs and wishes beforehand.
5. If a transfer to another care setting would be necessary for PST, ask if this would be an acceptable “trade-off”.
6. Ensure the patient and family understand the distinction between PST and MAiD.
7. Consult with ethics or conflict resolution services if needed, striving for consensus with the patient, family and health care team.

Document the following in the legal medical record that must be accessible to the inter-professional care team:

- Criteria for PST have been met.
- Patient, family and team discussions including decisions that were made
and their rationale.

- **Informed consent** by the patient or SDM.
- In addition to physician orders for sedation administration, a care plan with the following physician orders and directions must be accessible by all appropriate members of the care team:
  - Goal sedation level using the RASS-PAL scale. (Appendix B)
  - Schedule for monitoring of sedation level. (See Appendix C - medication table on monitoring guidelines for each medication)
  - Assessment for symptom control (e.g., nonverbal signs of discomfort).  
  - Other medications to be administered during PST.
  - Other treatments/interventions to be done during PST.

### PRINCIPLES OF MANAGEMENT

- The decision to use palliative sedation is informed through discussions with the patient, family members, and the inter-professional team
- Consult with an experienced palliative care physician/specialist to ensure all other symptom management options have been explored
- Consult with inter-professional specialists such as palliative social workers, counsellors and spiritual health practitioners when the patient has existential or emotional distress
- Provide ongoing patient, family, and staff emotional support
- Titrate to the minimum level of sedation to reach the goal for symptom relief
- Provide ongoing monitoring of sedation level and symptom relief
- Ensure adequate resources in the chosen care setting
- Document assessments, decisions, care plan and **informed consent**
Step 4 | Palliative Sedation Therapy

It is strongly recommended to seek consultation from an experienced palliative care physician/specialist and inter-professional team prior to initiating PST\(^1, 2, 3\) as well as for ongoing support and guidance for the duration of sedation.

Non-pharmacological:

- Ongoing assessment of patient comfort through facial expression or body language.\(^4, 23\) (Behavioral assessment tools for nonverbal or sedated patients may be helpful but have not been studied sufficiently for use with PST.\(^24\))

- Use the RASS-PAL (Appendix B) scale to monitor sedation level and titrate up or down to maintain goal level of sedation. Monitor frequency as per medication table (Appendix C).

- Provide the same care as for an unresponsive patient (such as mouth care and position changes, e.g., side-lying position to maintain patent airway\(^9\)), possible interventions for urinary retention\(^5, 7\) and bowel function.

Pharmacological (Appendix C -- detailed medication table):

1. Review current medications.\(^5, 6\)

2. Discontinue non-necessary medications in keeping with goals of care.\(^6\)

3. Opioids are not appropriate to induce PST.\(^3, 5, 9\)

4. DO NOT stop current medications for symptom relief as they will still be needed for optimal comfort (e.g., opioids for pain or dyspnea).\(^2, 5, 6, 7, 25\)

5. As consciousness is lowered, change all necessary medications to non-oral routes (may possibly use sublingual or buccal).\(^2, 5, 6\)

6. Determine any contraindications.\(^5\)

7. Most common medication classes used for PST are benzodiazepines, neuroleptics, barbiturates, or general anesthetics. Choices may depend on the expertise of the prescribing physician, medication availability, and the care setting.\(^3, 5, 6\)

8. Consider discontinuing previous benzodiazepines or neuroleptics if the same class will be used for PST purposes.

9. Titrate only to the level of sedation that is required for symptom control using the lowest dose to achieve comfort.\(^4, 5, 8\)
Patient and family education and support (see Appendix D -- recommendations for patient and family education materials):

- Before initiating PST, support the patient and family to do what is important to them such as rituals or saying goodbye as the patient will likely not awaken before natural death occurs.\textsuperscript{3, 9}
- Continue ongoing, frequent check-ins and emotional support with family members throughout the process from assessment, decision-making, initiation, during sedation, and following death.\textsuperscript{5, 6, 7, 9, 15, 22, 26}
- Discuss the usual signs and symptoms of impending death that may be misinterpreted as being caused by PST (e.g., altered respirations).\textsuperscript{2, 3, 9}

Staff support:

- Address the impact of bearing witness to suffering.\textsuperscript{3, 9, 26}
- Ensure they understand the background of the decision and have access to documentation of the decision-making process and care plan.\textsuperscript{6, 21}
- Ensure staff are confident and competent to provide and monitor sedation\textsuperscript{14} and have practice support as needed.\textsuperscript{9, 27}
- Provide opportunity for discussion and individual and/or team de-brief with all staff who may be involved with care of the patient and family before and during sedation, and after the patient’s death.\textsuperscript{4, 6, 9, 14, 27}
**APPENDIX A – DECISION-SUPPORT TOOL FOR REFRACtORY SYMPTOMS, PALLIATIVE SEDATION THERAPY (PST) AND CARE SETTINGS (SEE BODY OF THE GUIDELINE FOR BACKGROUND AND REFERENCES TO THE ITEMS BELOW)**

**Strongly recommended** to seek consultation from an experienced palliative care physician/specialist and inter-professional team

**DOCUMENT ASSESSMENT and BACKGROUND for all the items below:**

- Estimated time of natural death is within days.
- The patient is experiencing intolerable physical and/or emotional/spiritual suffering.
- All potential treatment options have been explored in consultation with an experienced palliative care physician/specialist and inter-professional team.
- The symptom(s) has been determined to be refractory/intractable rather than difficult because potential treatment options include one or any combination of the following:
  - Are incapable of relieving symptoms,
  - Have unacceptable side effects,
  - Require an unacceptable transfer to another care setting,
  - Would take an unacceptable length of time to be effective,
  - Are not in keeping with the patient’s goals of care, and/or
  - Are unacceptable to the patient and family for other reasons.
- Patient and family goals of care are consistent with a comfort end-of-life approach.
- Patient and family agree that PST is consistent with their current goals of care.
- Patient or SDM consent is documented.
All the following requirements for the care setting are met:

- Organization capacity and willingness to provide education, ongoing coaching and emotional support for patient, family and staff.
- Competent nursing support for the initiation, titration, stabilization of the dose and ongoing monitoring.
- Supplies and equipment for care of an unresponsive patient.
- Access to all anticipated medications and administration equipment for initiation, titration and maintenance of PST.
### Richmond Agitation-Sedation Scale - Palliative version (RASS-PAL)\(^9\)

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Combative</td>
<td>Overtly combative, violent, immediate danger to staff (e.g. throwing items); +/- attempting to get out of bed or chair</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes lines (e.g. IV/SO2/Oxygen tubing) or catheter(s); aggressive, +/- attempting to get out of bed or chair</td>
</tr>
<tr>
<td>+2</td>
<td>Agitated</td>
<td>Frequent non-purposeful movement, +/- attempting to get out of bed or chair</td>
</tr>
<tr>
<td>+1</td>
<td>Restless</td>
<td>Occasional non-purposeful movement, but movements not aggressive or vigorous</td>
</tr>
<tr>
<td>0</td>
<td>Alert and calm</td>
<td></td>
</tr>
<tr>
<td>-1</td>
<td>Drowsy</td>
<td>Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (10 seconds or longer)</td>
</tr>
<tr>
<td>-2</td>
<td>Light sedation</td>
<td>Briefly awakens with eye contact to voice (less than 10 seconds)</td>
</tr>
<tr>
<td>-3</td>
<td>Moderate sedation</td>
<td>Any movement (eye or body) or eye opening to voice (but no eye contact)</td>
</tr>
<tr>
<td>-4</td>
<td>Deep sedation</td>
<td>No response to voice, but any movement (eye or body) or eye opening to <em>stimulation by light touch</em></td>
</tr>
<tr>
<td>-5</td>
<td>Not rousable</td>
<td>No response to <em>voice or stimulation by light touch</em></td>
</tr>
</tbody>
</table>

Verbal Stimulation

Gentle Physical Stimulation
## Procedure for RASS-PAL Assessment

1. Observe patient for 20 seconds.
   - a. Patient is alert, restless, or agitated for more than 10 seconds  
     Score 0 to +4  
     **NOTE:** If patient is alert, restless, or agitated for less than 10 seconds and is otherwise drowsy, then score patient according to your assessment for the majority of the observation period.

2. If not alert, greet patient and call patient by name and say to open eyes and look at speaker.
   - b. Patient awakens with sustained eye opening and eye contact (10 seconds or longer).  
     Score -1  
   - c. Patient awakens with eye opening and eye contact, but not sustained (less than 10 seconds).  
     Score -2  
   - d. Patient has any eye or body movement in response to voice but no eye contact.  
     Score -3

3. When no response to verbal stimulation, physically stimulate patient by light touch e.g. gently shake shoulder.
   - e. Patient has any eye or body movement to gentle physical stimulation.  
     Score -4  
   - f. Patient has no response to any stimulation.  
     Score -5
## APPENDIX C – MEDICATION TABLE

Seek palliative care physician/specialist support if desired level of sedation is not reached with maximum doses or unacceptable side effects occur.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial / loading dose</th>
<th>Titration</th>
<th>Usual maintenance dose</th>
<th>Route of administration</th>
<th>Monitoring</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>1-5 mg(^2, 3, 5)</td>
<td>0.2-1 mg/hr</td>
<td>1-10 mg/hr(^2, 5)</td>
<td>Continuous or intermittent SC or IV</td>
<td>With each titration, Q30 min until goals are reached and maintained for 1 hr. then Q4-8H(^5)</td>
<td>Intermittent dosing is not recommended due to the short half-life</td>
</tr>
<tr>
<td></td>
<td>Usually 2.5-5 mg</td>
<td>Titrate up or down Q10-30 minutes(^2, 5)</td>
<td></td>
<td></td>
<td></td>
<td>Delirium or agitation is a rare complication(^5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Start with a low dose and titrate up as needed, especially with elderly and/or low weight patients(^3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrimeprazine</td>
<td>5-25 mg(^5)</td>
<td>5-25 mg Q8H and Q2H PRN to max 25 mg Q6H(^5) 50 mg Q6H and up to 300 mg/24 hrs.</td>
<td>SC</td>
<td>Q1H until goals are achieved then Q8H(^5)</td>
<td>If used in combination with Midazolam, monitor as per Midazolam(^5) Use with caution in renal and hepatic dysfunction(^3)</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Initial / loading dose</td>
<td>Titration</td>
<td>Usual maintenance dose</td>
<td>Route of administration</td>
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<td>Notes</td>
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<tr>
<td>Phenobarbital</td>
<td>Depends on degree of sedation 30 mg, 60 mg, 90 mg or 120 mg&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very long half-life (53-118hrs)&lt;sup&gt;5&lt;/sup&gt; 30-120 mg SC/IV BID-TID</td>
<td>Max. 720 mg/24H&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Deep SC, may also use continuous subcutaneous infusion – less tissue necrosis and burning</td>
<td>Q1H until goals are achieved then Q8H5 Monitor for respiratory depression&lt;sup&gt;6&lt;/sup&gt;</td>
<td>If used in combination with Midazolam, monitor as per Midazolam&lt;sup&gt;5&lt;/sup&gt; It can potentially decrease effectiveness of midazolam (requires close monitoring of sedation) Mostly used for deeper levels of sedation, use with caution if the goal is light sedation&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Medication</td>
<td>Initial / loading dose</td>
<td>Titration</td>
<td>Usual maintenance dose</td>
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<tr>
<td>Lorazepam(^3,^6)</td>
<td>0.5-1 mg(^3) SC or IV 1-4 mg sublingual / buccal(^3) Buccal not often used due to inconsistent absorption</td>
<td>0.5-2 mg Q2H PRN (^3)</td>
<td>1-4 mg SC / IV Q2-4H or 1-8 mg sublingual / buccal(^3)</td>
<td>SC / IV or may start with sublingual or buccal(^3)</td>
<td></td>
<td>Is on the B.C. formulary and used occasionally. Anecdotally effective when the patient goal is to be in an altered mental state but not sedated per se, e.g., wishes to eat and drink</td>
</tr>
<tr>
<td>Dexmedetomidine(^8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>As per agency policy(^5,^6)</td>
</tr>
<tr>
<td>Propofol(^3,^5,^6)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
APPENDIX D – RECOMMENDATIONS FOR PATIENT AND FAMILY PRINTED MATERIALS

The information below is not intended to be printed and handed out. Rather, it is to be used as a guide to develop organization-specific materials. Follow your organization’s policies and procedures for developing patient and family education materials.

*Italicics indicate possible phrasing which was developed for B.C. by consensus of palliative experts and limited consultation with patient and family representatives; however, there was no consultation with experts in health communication.*

Recommend eliciting significant patient and family feedback and evidence-based development of appropriate language including literacy level.

1. **Introduction** – it is difficult to see someone you love suffering, or to suffer yourself.

2. **Definition of Palliative Sedation Therapy (PST)** – PST is medication given to make a person not alert, to sleep, less able to rouse, and comfortable, so they aren’t suffering.

3. **Distinguish PST from MAiD** – PST is different because:

   4. **PST Is only offered when a person is not able to be comfortable with other interventions.**
      
      a. **PST is only offered if a person is expected to die soon.**
      
      b. **When a person is sedated with PST, they die naturally from their illness. When a person is given MAiD, they die from the medication.**
      
      c. **A person must be alert and competent to consent for themselves for MAiD, whereas a SDM can consent for PST on the person’s behalf.**
      
      d. **The exact timing of death within days and hours is not known with PST and is more predictable with MAiD.**

   If you wish to consider MAiD, we can provide you with information and access to decision-support.

4. **When would PST be offered?** – PST is offered when everything else has been tried to help the person dying of their illness to be comfortable and all other options:

   a. **Cannot help with the symptom.**
b. Have unacceptable side effects.

c. Would take too long to work.

d. Do not fit with what you and your loved one want.

e. Cannot be given in your preferred care setting and a transfer is not what you want.

5. Decision-making process - The patient, family, physician and other health care team members will decide together if PST is the best option. PST will only be offered if:

a. The illness is serious and a natural death from that illness is likely soon.

b. Suffering is unbearable and unmanageable.

c. It fits with patient and family goals for care and for remainder of life.

d. The person and/or their SDM understands the risks and benefits and gives informed consent.

6. What is expected if PST is initiated?

a. The person will die as they would have, except they will be more comfortable.

b. You will see the usual changes as someone dies (describe skin mottling, etc.)

c. A decision will be made with the patient, family and health care team about the goal sedation level and only enough medication to reach that goal will be given.

d. The nurse and doctor will work together to find the right dose to reach the goal.

e. Nurses will regularly monitor the person to make sure they are comfortable without being too sedated.

f. The patient and family will be supported emotionally throughout the decision-making and PST process.
REFERENCES


3. Fraser Health Hospice Palliative Care Program. Refractory Symptoms and Palliative Sedation Therapy Guideline. 2011; Available from: https://www.fraserhealth.ca/employees/clinical-resources/hospice-palliative-care#.XGXBmuhKg2x


